Is Covid19 a TRMP7 derangement syndrome ?

In Mar 2020 I got interested into Magnesium as a means to modulate covid19 hypercytokinemia. I encouraged relevant people to roll-out a world-wide magnesium resiliencing program, obviously with zero result. Now, I reviewed the TRMP7 literature since 2019...

Inhibitors of TRPM7

Ginsenoside Rd; Ginseng				31947967, 33143990
Astrogaloside IV	Astragalus membranaceus: Fish			
NS8593				32146159
FTY720				31545149
Sacubitril				34778271
TG100-115				33658993
Var. NSAR	Naproxen, Ibuprofen, Salicylate, ASS	Cytosolic acidification		34733174
Progesterone				31293101
2-apb	2 amino ethyl diphenyl borate			31947967
Camp:pka				30615643
CCT128930				33989904
CFTR Mutation	Cystic fibrosis			31176886
Pantoprazol				34714373
Gadolinium	Gd(3+)			32468675
Magnesium				Common

				sense
Lidocain				33435261
Carvacrol	Origanum vulgare			32337263, 31848974
Oridonin				34285910
Waixenicin A				31219801, 32994545
Rikkunshito	Japan herb			30889598
Mir-22-3p				32924998
Mir-129-5p				33951695
Mir-135a				31739105
Mir-149				33284571
Mir-204-5p				32484206
Mir-192-5p				34042256
Mir-543				30710498

Activators of TRPM7

Cobalt				30523498
HULC	Spongt mir-204-5p			32484206
Naltriben				32146159
Leptin				31545149, 33891828

Stretch, shear stress				31921825, 34244134
Elastokine	RPSA rec			32733880
Isoproterenol				32390858
Hypoxia				32215176
Acidosis				31293101
Cadmium				32080757
Clozapin				34752845
Bupivacain				34060177
H2O2				33999118
LPS Endotoxin		TLR4 NOX2 R.O.S. NF kappaB	Tnfa, il1b, il6, il12	31444399, 31288723
Phosphat				32800835

Major pathophysiological concepts with TRPM7 involvement

Sepsis				32484206
Acute renal failure				31060485
Endothelium and Inflammation				
Inflamma-some				33951695
(Endothelium and Coagulation)				NOTHING

Fibrosis EMT TGFbeta Cancer Migration Invasion				33456540, 30819230, 32047249, 33143990, 33647257
Osteogenese, Amelogenese				32596398, 33924361
Tumormatrix	ChondrSO4 PG			30453391
Hypertension				31219801 33494094
Endothelial barrier				31559137
Epithelial barrier				
Blood brain barrier				33114331
Neurotox Neuroresil				33029295
NETosis				NOTHING
MDSC				NOTHING
PMN	Mig, R.O.S.			33658993
Macrophage	M1			33153718
Zellvolumen				34017036

Major downstream pathways

Cobalt influx	hif1a			30508321
P38, JNK				33494094
Cytoskeleton	rhoA			31844251

Zinc influx	tox			33114331
Calcium influx	RhoA, cdc42, iqgap1, calmodulin, myosin-ii			34244134
O-GlcNAc				32684624
Caveolin				32684624
c-myc				32684624
Akt; mTor				33658993, 30819230
Hedgehog				33927631
notch1				33381038
stat3				33381038
Cd133, ldh1	stemness			33381038

Active complex structure

TRMP7				
Other TRMP				
EGFR, c-src				32706027
CNNM1,2,3,4	Metal transp			34766907
ARL15	g-protein			34766907
mdmx	zinc			34627839

The tables show raw data from all relevant abstracts on TRPM7, so, where is the overlap, where is absolute lack of knowledge, which substances are available for retargeting approaches.

Center stage is the sepsis-vasculitis aspect of covid19 disease at microvascular location with a multitude of organs under possible attack. TRPM7 is expressed ubiquitously.
On the long-term, TRPM7 activity makes „bones from viable tissues“, organ fibrosis and vascular sclerosis and persistent microinflammation.
On the short term, TRPM7 shifts Calcium into any cell which leads to the activation of a couple of signal transduction pathways ultimately „activating“ it.
There is lack of published data on the central nexus around endothelial dysfunction – inflammothrombosis which causes the extrapulmonary major complications of covid19 disease.
We have to assume that a system which disturbs the endothelium in a sepsis like mode with TRPM7 at nexus point should produce that set of weibel-pallade bodies, adamts13, thrombomodulin, complement in situ, ros, local platelet and neutrophil adhesion which makes the ultimate thromboses and embolisms.
Same tissue activation should run into the diseased respiratory epithelia and deep airways.

There is currrently not one paper which looks into TRPM7 involvement in covid pathology material so follow-the-science depends on rational imputation. I emailed some authors which are active in TRPM7 to apply their established methods to human or animal specimens.

Acute as well as the long Covid should be treated at TRPM7, in the acute setting as add-on, in the chronic setting in basic antifibrotic intention.

Magnesium supplementation is the absolute bottom method to inhibit TRPM7 and it shows additional effects, and, Mg2+ cannot be understood w/o TRPM7.

I got really excited as I read about **Sacubitril** since it is in clinical use in the indication of HfrEF, so roll-out would not be a problem.

Is THIS a paper – quite not. It will grow as I read the papers and so on. Numbers given are PubMed Identifiers, access item by

http://www.kidney.de/pget.php?pmid=34519155 and so on.

A trial of Sacubitril/Valsartan is running at Duke
https://www.clinicaltrials.gov/ct2/show/NCT04883528

Author (me) Ossip Groth, Lepser Strasse 54, 39261 Zerbst (Germany)

My major resources are

www.coviki.org – Covid19 literature database
www.moremed.org – literature search house PubMed, PMC and many others.
www.bdom.kidney.de – up to 2011 vintage medical review collection
https://archive.org/details/@ossip_groth - something

On the question of Magnesium supplementation – working hypothesis give Amiloride

New study shows, more hypermagnesiemia – more severe covid disease. This frustrated me to conclude that the problem is magnesium redistribution from intracellular to extracellular, so, lower intracellular magnesium would lead to trmp7 overactivity.
Clinically, ACEIs/AT1RAs come with plus: Hydrochlorothiazide which extrudes Magnesium from the intracellular space while Amilorid(e) „potassium saving diuretics concept“ inhibits cellullr magnesium egress, so, merely than overeating magnesium, at least covid patients should add Amiloride. I have not read the papers yet, and the biblio will follow. Only to state my claim on nov 29th 2021.